

### REMARKS

The present invention is directed to compositions that have one to two physical properties that are nano-scale dimensions. More particularly, the compositions have at least one property selected from the group consisting of grain size, particle size or surface roughness that are less than 500 nanometers. The claims have been amended to clarify the claimed invention and more particularly claim that which applicants believe to be their invention. The amendments to claim 1-11 are not believed to be substantive in nature and are intended to clarify the abbreviation "nm rms" and use consistent terminology. New claim 12 is directed to a composition that has nano-sized particles of less than 500 nm, and new claims 13-16 are directed to a composition having nano-sized particles of less than 500 nm and a surface roughness between 11 and 356 nm rms. Support for those new claims is found in paragraphs [0008] and [0010].

Claims 1-4 and 8-11 stand rejected under 35 USC 103 as being obvious over the teachings of Yadav et al (US patent no. 6,572,672). Applicants respectfully traverse this rejection.

The Examiner notes that Yadav et al discloses forming metallic orthopedic devices from powders having grain sizes less than 500 nm. However, the reference is devoid of any teaching or suggestion regarding the desired surface roughness or the particle size of the compositions. Claim 1 of the present invention requires the biomaterial to not only have a grain size of less than 500 nm, but also requires a surface roughness of less than about 500 nanometers root mean square (nm rms). Applicants respectfully submit that surface roughness is not necessarily directly correlated with grain size. Accordingly, the disclosed metallic material of Yadav et al, while comprised of nano-sized grains, does not inherently have a surface roughness of less than about 500 nm rms contrary to the Examiner's assertion. Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient (*In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)

In support of applicant's position, transmitted herewith is a publication by Woodcock et al, which states that similar grain sizes can produce different surface roughness based on the orientation of the grains. In particular, see Figure 6 which shows the same grain sizes oriented in a different manner comparing the left to the right of the AFM image. On the right, the grains are perpendicular (sticking out) and on the left they are parallel to the surface. The paper goes on to say (as can be clearly seen) that these two different regions on the AFM have different roughness. Accordingly, applicants respectfully submit that the mere designation that a material is comprised of nano-sized grains fails to specify a particular surface roughness for that material.

Applicants have found that a metallic implant that displays both a surface roughness of less than 500 nm and having a grain size of less than 500 nm have superior biocompatibility and improved osteoblast adhesion.

Furthermore, applicants have found that compositions formed from nanoparticles also exhibit surprising properties. As noted above Yadav et al is devoid of any teaching or suggestion regarding the preparation of materials that display surface roughness of less than 500 nm rms and/or comprise nanoparticles of less than 500 nm. Each of these physical properties are separate and distinct from the grain sizes disclosed in Yadav.

Transmitted herewith is an article by Nelson and Deng that clearly demonstrates that those skilled in the art appreciate that grain size (crystal size), particle size and surface roughness are three separate and distinct physical characteristics of a material. Furthermore, alteration of any one of these properties can impact the physical properties of the material. In particular, we note page 134 of the Nelson and Deng article, column two, the first two full paragraphs, wherein the authors state that the grains (i.e., crystals) are the composite materials that form particles. In their concluding remarks the authors state, "In conclusion, it was found that the efficiency of rutile pigments can be increased dramatically by controlling both the primary crystal size and the overall particle size." (page 139, second column last sentence). Accordingly, long after applicants had filed their application, investigators disclose that modification to grain size as well as particle size both impact the physical properties of the resulting material.

Applicants have made the surprising discovery that osteoblast adhesion at the metal/tissue interface can be increased by utilizing nano-particle metals and nano-surface roughness materials. More particularly, metals having nanosized particles of less than 500 nm and a surface roughness between 11 and 356 nm rms display an enhanced level of osteoblast adhesion (see paragraph [00015] and [00016] of the application as filed) relative to

standard materials. In addition, applicants also submit two separate Declarations under 37 CFR 1.132 by Dr. Webster (previously submitted in related US patent applications), with the relevant accompanying supporting data. These declarations demonstrate the surprising properties associated with materials exhibiting nanoscale dimensions relative to sub-micron and micron-sized dimensions.

The Yadav reference is devoid of any teaching or suggestion with regards to particle size and/or surface roughness. Furthermore, the reference fails to suggest that altering the particle size or surface roughness of a metal to nano-sized proportions would improve osteoblast adhesion to such a surface. Applicants have described a novel biomaterial that exhibits unexpected properties (e.g., enhanced osteoblast adhesion). Accordingly, the claimed invention is believed to be patentably distinct over the teachings of Yadav et al., and applicants respectfully request the withdrawal of the rejection of claims 1-4 and 8-11 for obviousness.

Claims 5-6 stand rejected under 35 USC 103 as being obvious over the combined teachings of Yadav in view of Oshida (US Patent no. 6,183,255). Applicants respectfully traverse this rejection.

The deficiencies of the Yadav disclosure with regards to the claimed invention have been discussed above. Claims 5 and 6 ultimately depend from claim 1 and thus incorporate all the limitations of the base claim. The secondary Oshida reference fails to supplement the deficiencies of the Yadav reference with regards to the disclosed use of materials that have a surface roughness of less than 500 nm rms and/or are comprised of particles having a size of less than 500 nanometers. Accordingly, the combined teachings of Yadav and Oshida fail to teach or suggest the present invention. The invention of claims 5 and 6 is believed to be patentably distinct over the teachings of those references and applicants respectfully request the withdrawal of the rejection of claims 5 and 6 for obviousness.

Claim 7 stands rejected under 35 USC 103 as being obvious over the combined teachings of Yadav in view of Davidson (US Patent no. 5,415,704). Applicants respectfully traverse this rejection.

The deficiencies of the Yadav disclosure with regards to the claimed invention have been discussed above. Claim 7 depends from claim 1 and thus incorporates all the limitations of the base claim. The secondary Davidson reference fails to supplement the deficiencies of the Yadav reference with regards to the disclosed use of materials that have a surface roughness of less than 500 nm rms or are comprised of particles having a size of less than 500 nanometers. Accordingly, the combined teachings of Yadav and Davidson fail to teach or

suggest the present invention. The invention of claims 5 and 6 is believed to be patentably distinct over the teachings of those references and applicants respectfully request the withdrawal of the rejection of claims 5 and 6 for obviousness.

Applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read "John P. Breen", with a long, sweeping horizontal stroke extending to the right.

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